

BLOOD SUPPLY CHANGE IN THE AREA OF THE  
LOWER EXTREMITIES AS RESULT OF INACTIVITY AND  
ITS CONTROL BY TRASYLOL

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im Bereich der unteren Extremitaet infolge Inaktivitaet  
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NOTICE

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BLOOD SUPPLY CHANGE IN THE AREA OF THE  
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The circulation deceleration in the area of the lower extremities in the /2822\* case of lengthy immobilization — such as caused by trauma or after operations — has been repeatedly demonstrated by clinical observations and clinical-experimental investigations [1-6] and discussed as to their significance for post-operative action [7-9]. Figure 1 summarizes and illustrates findings of various authors on this matter.

With respect to timely and therefore optimum countermeasures, it appeared of special significance to us to make a determination when these circulation changes take effect from the clinical point of view.

Experimental Arrangement and Methodology

For this reason, we carried out model-type experiments under standardized conditions on 10 healthy test subjects during immobilization periods lasting more than 8 hours. During these periods measurements were made of the circulation in the area of the lower extremities. The first measurement took place after one hour of inactivity with further measurements made at one hour intervals until the 8th hour.

Following determination of the standard values or curves valid for them, these same test subjects received 400,000 E trasylol 10-14 days later following a renewed determination of the initial value. The first measurement with trasylol took place after one hour.

Individual measurements were made of:

1. The blood supply using vein occlusion plethysmography.

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\*Numbers in the margin indicate pagination in the foreign text.

2. The reestablishing force (tonus) of the peripheral venous vascular system during compressive load.

3. The residual volume after a compressive load.

Both of the last two measurements allow conclusions to be made concerning the operating efficiency of the venous storage.

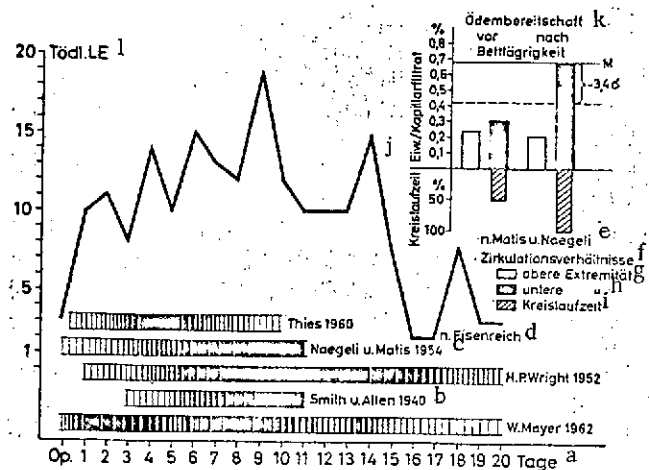


Figure 1. Circulation and Deceleration in the Area of the Lower Extremities when Bedridden. The horizontal strips correspond to the increase always observed in the (partial) circulatory time in postoperative behavior. With an increasing circulation deceleration the susceptibility to edema increases (upper right). The curve provides the frequency of postoperative fatal pulmonary embolisms of one clinic (10) [according to (9)]. a, Days; b, Smith and Allen 1940; c, Naegeli and Matis 1954; d, according to Eisenreich; e, according to Matis and Naegeli; f, circulatory conditions; g, upper extremity; h, lower extremity; i, circulatory time; j, circulatory time with albumin/capillary filtrate; k, susceptibility to edema before and after immobilization; l, fatal pulmonary embolism.

abscissa corresponds to a decrease in the residual volume.

For this reason, the customary method for displaying pressure-volume curves was modified. The corresponding methods of pressure and volume in the peripheral vascular area of the human in the leg, both in the case of increase in venous internal pressure as well as in the case of the consequent drop in pressure, was continuously recorded using a X-Y plotter. We designated the curves in this manner as the pressure-volume loop (11). The surfaces between the curves and the ordinates up into the high points of the systolic pressure or loop surfaces were measured planimetrically. Volume/residues after release of pressure can be read off directly on the abscissa. A decrease in the measured surfaces indicates an increase in tonus or reestablishing force of the venous system whereas a decrease in size of the section on the

Figure 2 first of all shows an example of the behavior of the pressure-volume loop both in the zero-experiment as well as in the case of periodic application of trasylol at four hour intervals.

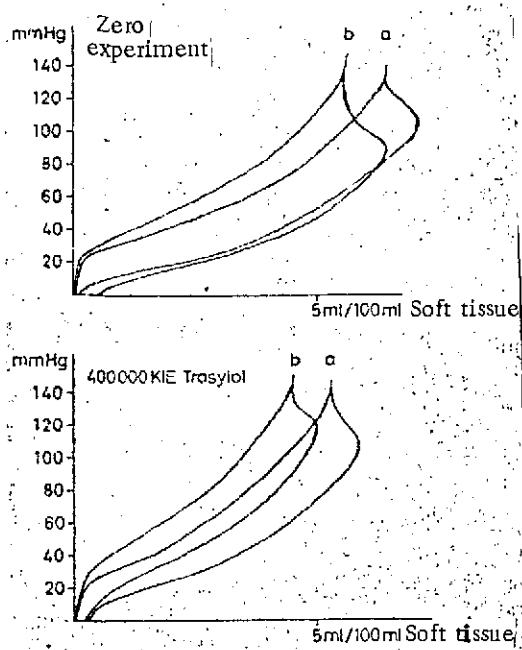


Figure 2. Pressure-Volume Loop of a Test Subject Both in the Zero-Experiment (Above) as Well as with Application of 400,000 E Trasylol After Beginning of the Test (Below). a, Initial curves; b, pressure-volume loop 4 hours after beginning the test. Ordinate, dynamic pressure at the upper part of the thigh; abscissa, corresponding increase in volume of the thigh in ml/100 ml soft tissue.

Whereas an increase in the loop surface or loop content is only found after an immobilization after 4 hours, the application of trasylol leads to no enlargement of the loop surface. This means that the functional or operating efficiency of the venous storage is affected by the drug in such a way that the stored up volume is led off just as quickly as at the beginning of the experiment. /2823

The individual curves of the 10 test subjects are summarized in the following figures whereby common display forms have been selected.

The vertical lines signify in each case the quantity of the mean error of mean value  $\bar{Sx}$ . In order to eliminate the individual dispersion, the initial points of the individual curves were shifted to a common mean

value. The second-order equalizing parabolas of the respective curves are (as much as possible) plotted with the specifications of the equations. The reference index p provides in each case the probability with which the two corresponding measurements agree with one another. In the case of  $p \leq 0.05$ , this agreement no longer exists.

## Results

Behavior of the Blood Supply. Figure 3 shows how the blood supply in the area of the lower extremities continues to decrease in the course of 8 hours as

the result of immobilization (standard curve A). After application of trasylol (curve B) a significant increase in blood supply ( $p \leq 0.01$ ) is noted with blood remaining constant. This reaches a peak after one hour. It remains for 3-4 more hours above the initial value only to again return to the values corresponding to normal behavior towards the end of the experiment.

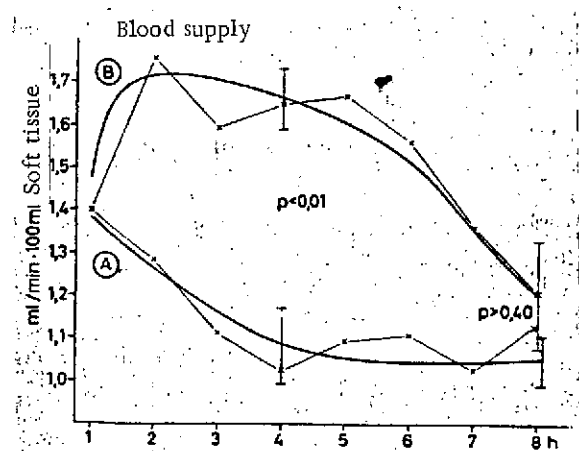


Figure 3. Behavior of the Blood Supply Without (A) and With (B) Trasylol. The test subjects remained quiet for 8 hours in an environmental chamber. Their lower extremities were immobilized on rails. Abscissa, time and hours; ordinate, blood supply in ml/min per 100 ml soft tissue.

#### Behavior of the Venous Storage During Compressive Load

It can be seen from Figure 4 that the surface contents of the loops during the period of immobilization increase in the case of the untreated subject (standard curve A). This means a loss of the reestablishing force of the venous storage in the direction of a tonus loss alone through consequent immobilization. This characteristic increase (curve B) is not found after application of trasylol. The difference with normal behavior is significant ( $p = 0.01$ ).

#### Behavior of the Volume Residue After Compressive Load

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The volume residue recorded after the respective measurement can be seen from Figure 5. This residual volume increases alone through the consequent immobilization. It is not affected by trasylol.

#### Summary

Our observations show that significant changes in circulatory behavior occurs even in the very first hours of an inactivity on the part of the lower extremities. This is expressed in the following measured quantities:

1. A decelerating increase in blood supply.
2. An increase in input into the venous storage corresponding to a loss of reestablishing force of the peripheral venous system in the direction of a decrease in the peripheral reflux requirement.

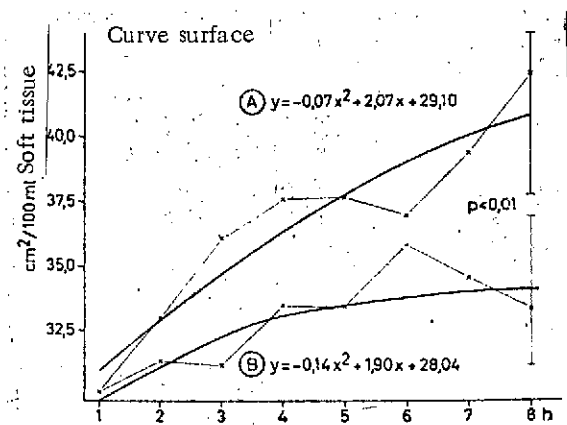


Figure 4. Behavior of the Venous Storage Area Without (A) and With (B) Trasylol. The test subjects remained quiet for 8 hours in an environmental chamber. Their lower extremities were immobilized on rails. Abscissa, time and hours; ordinate, surface of the pressure-volume loop in  $\text{cm}^2/100 \text{ ml}$  soft tissue (X-Y plotter calibration:  $23 \text{ cm X } \underline{\Delta} 20 \text{ ml}$ ;  $16 \text{ cm Y } \underline{\Delta} 100 \text{ mm Hg}$ ).

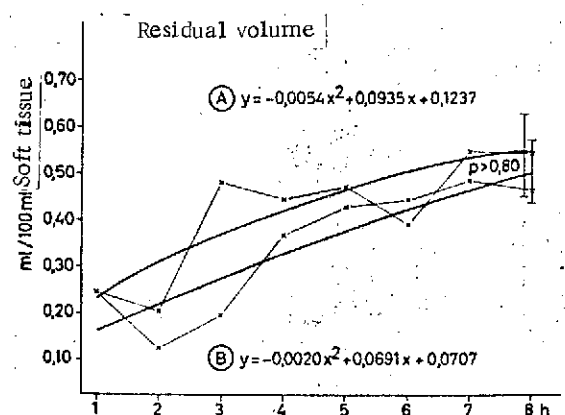


Figure 5. Volume Residue after Compressive Load Without (A) and With (B) Trasylol. The test subject lies quiet in the environmental chamber for 8 hours. The lower extremities are immobilized on rails. Abscissa, time and hours; ordinate, residual volume in  $\text{ml}/100 \text{ ml}$  soft tissue after a compressive load lasting for 10 minutes.

### 3. An increasing susceptibility to edema.

On the other hand, we found that after one application or 400,000 E Trasylol i.v. under generally similar experimental conditions using the same test subjects:

1. An increase in the blood supply without modification of the peripheral resistance (blood pressure).
2. The preservation of the operating efficiency, meaning reestablishing force, of the venous storage in the direction of an unaffected reflux requirement.
3. The residual edema appearing under the measurement conditions remains unaffected.

The effect of the trasylol leading to an improvement in circulation consequently contributes effectively to the equalization of the hemodynamic prejudice of the lower extremities with all consequences.

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